REMARKS

The claims have been amended to limit them to the elected invention. Claim 1 has been amended to read on embodiments which contain a piperazine ring. Claims 10 and 13 have been canceled as redundant and claim 14 is canceled as directed to a non-elected invention. Claim 38 has been amended to delete compounds that do not fall within the scope of the currently claimed invention. Claims 39 and 42 have been amended to depend from claim 1 rather than spelling out the structure once again. Claim 44 has been amended to delete the objected-to indications of septic shock, stroke and CNS injury in order to simplify prosecution. It is believed these indications are already covered by claim 42 to the extent they are mediated by p38 kinase. The objected-to indication of cardiac disease does not appear in this claim.

No new matter has been added and entry of the amendment is respectfully requested.

It is noted that in the original restriction requirement, claim 39 was not listed as a part of any group. As this claim appears to have been examined, and as it is directed simply to a pharmaceutical composition of the compounds of claim 1, it is believed that it is appropriate to include this claim. Claims 40-41 have not been canceled as they depend from claim 39 and their patentability does not depend on the presence of the additional therapeutic agent referred to in these claims. Therefore, applicants respectfully request that these claims remain examined in the application.

It is believed that the amendment and foregoing discussion address the objection set forth on page 2 of the Office action.

Rejections Under 35 U.S.C. § 112, Paragraph 1

The rejection of claims 42-44 based on the inclusion of treating stroke, CNS injury or heart disease has been addressed by amendment and discussion. Heart disease does not appear in

this claim; reference to CNS injury and stroke have been deleted, thus obviating this basis for rejection. A similar rejection was made with regard to claims 42-44 based on the inclusion of septic shock. This indication, too, has been deleted from the claims, thus obviating the basis for rejection.

The Rejections Under 35 U.S.C. § 112, Paragraph 2

The various rejections made under this section will be addressed in the order in which they have been presented.

a. The term "non-interfering substituents" is objected to as not clear in claim 1. However, this term would be understood as substituents that do not interfere with or destroy the ability of the compounds to inhibit p38-α kinase. This is spelled out on page 5 of the application, beginning at line 3. As there noted, there are a number of convenient assays for determining the ability of a compound to inhibit p38-α activity and thus one could readily test whether a given substituent would or would not interfere with this activity. Those that destroy the ability to inhibit this kinase would be shown to be interfering substituents and not included within the scope of the claims; those which result in the compound retaining its inhibitory activity would be identified as non-interfering.

On need not guess wildly at what kinds of substituents might be non-interfering as the specification makes multiple suggestions for such substituents, for example, on page 11, at line 7, and page 9, at line 11. Ordinarily skilled artisans would understand the nature of substituents that are unlikely to interfere with the inhibitory activity of these compounds and any substituent selected from within this group can readily be tested to verify its non-interfering character. Therefore, it is respectfully submitted that this term is not indefinite.

b. Similarly, applicants believe that L^1 and L^2 defined as linkers is sufficiently definite in view of the suggestions made in the application for their nature and in view of specifying the maximum distance between Ar and the center of the β ring. This distance is, in terms of the end points, defined precisely on page 6, line 29-page 7, line 1. Various suggestions for the nature of these linkers if found on page 7, beginning at line 1 and continuing to line 21. In view of this specificity, it is believed these terms are clear.

c. Similarly, the definitions of W and X as spacers is believed definite as the distance bridged by the spacers is defined precisely in the claim and, again, the nature of spacers that would appropriate is suggested on page 10, beginning at line 29.

d. In response to the objection to the phrase "for treating conditions characterized by enhanced p38-α activity" – this phrase has been removed from the claim. And the suggestion kindly made by the Examiner for rewording has been adopted.

e. The reference to claim 57 is believed to be in error. As to claim 42, the invention lies, in part, in the discovery that the novel compounds of the invention are inhibitors of p38-α kinase. Some of the conditions which are thus mediated have been identified in claims 43 and 44; however, the nexus between this kinase and various additional conditions may not have been determined at this time. Applicants believe they are entitled to the full scope of their invention, and the temporal accident whereby the nexus has been identified for certain conditions, but not others, should not result in a narrower claim scope than that to which applicants are entitled.

In any event, it is within the skill of the art to ascertain in an individual, regardless of what might be considered commonplace, identified conditions, whether the activity of p38-α

kinase in that individual is too high. Assays for such activity are known as is indicated on page 5.

The concerns described by the Office are well founded; however, identification of the appropriate subject does not depend on the nature of the response of that subject to the compounds of the invention, but rather on whether p38-α kinase activity is elevated. Accordingly, it is believed that claim 42 is clear and applicants respectfully request that this basis for rejection be withdrawn.

Applicants note with appreciation that the claims are patentable over the art.

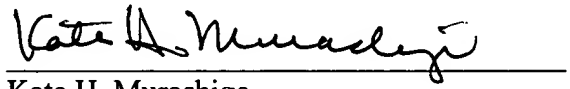
CONCLUSION

With respect to claims 1-13, and 15-39, only objections under 35 U.S.C. § 112, paragraph 2, are applied. The foregoing amendment and discussion deals with these rejections. Claims 42-44 were rejected for lack of enablement only on the basis of the indications of heart disease, stroke, CNS injury and septic shock. These indications do not appear in the claims any longer.

None of the claims are rejected over the art. Accordingly, it is believed that the now-pending claims, claims 1-9, 11-12, and 15-42 are in a position for allowance. Should formal matters remain to which the Office objects, a telephone call to the undersigned would be appreciated. It is quite possible that formal matters may be worked out over the phone without the necessity for an additional official action.

In the unlikely event that the transmittal letter is separated from this document and the Patent Office determines that an extension and/or other relief is required, applicants petition for any required relief including extensions of time and authorize the Assistant Commissioner to charge the cost of such petitions and/or other fees due in connection with the filing of this document to **Deposit Account No. 03-1952** referencing docket No. 219002029300.

Respectfully submitted,

Dated: July 31, 2003 By: 

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